ABSTRACT

Objective: The purpose of this study was to compare the use of benzocaine, lidocaine, tetracaine (BLT) cream with and without abrasive particles to see which type of cream is more effective in reducing discomfort during cosmetic dermatologic procedures, specifically procedures using hyaluronic acid (HA) injectables. **Methods:** The study was conducted as a single-site, double-blind, paired study. **Participants:** Thirty-one subjects were enrolled. Men and women over 18, but not more than 75 years of age, were included. Participants were randomized to receive two types of BLT creams in a split-face fashion to two opposite anatomical face locations that require a similar amount of filler. **Results:** The study found a statistically significant difference ($P<0.05$) in the mean pain level as measured by the VAS and Wong-Baker Faces Pain Rating Scale when compared between baseline and the time when the procedure was started at the first needle stick. Subjects expressed significantly less pain with baseline and more pain when the procedure was done. However, the authors found that the mean pain level at first needle stick is lower with the abrasive type of BLT. **Conclusion:** The study demonstrated that subjects experienced a higher mean pain level (but not statistically significant) when using the BLT with smooth texture compared to the BLT with abrasive particles when applied before HA dermal filler injection.

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ORIGINAL RESEARCH

Comparative Study of Compounded Anesthetic Benzocaine/Lidocaine/Tetracaine (BLT) Cream with and without Abrasive Particles

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Minimally invasive cosmetic procedures are now growing in popularity. Injection of dermal fillers for soft tissue augmentation is one of the most popular cosmetic procedures.[1] Patient discomfort is an important consideration in aesthetic procedures, as is fear of needles because it may cause anxiety in patients who are awaiting procedures in the outpatient seating. More effective topical anesthesia is particularly sought after by patients undergoing these treatments. Furthermore, pain ranked third in determining patient satisfaction and willingness to undergo skin rejuvenation treatments.[2]

Nowadays, anesthetic mixtures are commonly used before outpatient dermatologic procedures to improve tolerability. These local anesthetics may be associated with a narrow margin of safety in some patients. Since compounded topical anesthetics have become increasingly popular, there are several challenges related to their safety.[4] Application guidelines for these compounded topical anesthetic creams are still lacking at this time.

Numerous lidocaine-containing products are available. One of the most popular formulations is the benzocaine, lidocaine, tetracaine (BLT) compounded mixture. BLT comprises active ingredients of 20% benzocaine, 8% lidocaine, and 4% tetracaine and is compounded by specialty pharmacies for physicians to purchase. There have been some concerns raised about the safety of BLT because of its higher concentrations of compounded

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anesthetics than those found in the United States Food and Drug Administration (FDA)-approved products.[5,6]

Although there are several studies regarding lidocaine-containing topical anesthetics, up to now, there are no known controlled studies that have directly compared the safety and efficacy of the compounded anesthetic formulation of BLT cream.[5] BLT is a specially compounded mixture of powdered forms of abrasive particles that are mixed together in an oil base. Clinicians routinely use two main types of BLT: a smooth type and a coarsely textured type caused by abrasive particles that have not dissolved completely in the compounded mixture. Some clinicians prefer the abrasive type because they feel that when it is rubbed into the skin, the particles cause the cream to penetrate the skin more thoroughly to provide greater anesthesia than the smoothly textured type of BLT. However, the coarse texture of the anesthetic can cause it to penetrate into delicate structures of the eye and cause serious mechanical or chemical irritation to the cornea. A case report has cited adverse events related to the use of BLT penetration into the eye and possible injury to the cornea.[7] To the authors' knowledge, there were no comparative studies of BLT compounds available in the literature. With this study, they speculate that although there may be no clinically statistical differences between the two types of BLT creams in terms of clinical efficacy, it may be safer to use BLT without abrasives to minimize the potential for side effects.

Figure 1. BLT used in the study (left: abrasive; right: smooth)

OBJECTIVES

The purpose of this study was to compare the use of BLT cream with abrasive particles (pharmacy A) and without abrasive particles (pharmacy B) (Figure 1) to see which type of cream is more effective in reducing discomfort during cosmetic dermatologic procedures, specifically procedures using hyaluronic acid (HA) injectables. The authors hypothesize that there may not be a significant difference between the two types of BLT creams in terms of clinical efficacy; however, the smooth type of BLT without abrasives could be the safer type to use in terms of causing less side effects, such as potential risk of ocular injuries. The efficacy of BLT topical anesthetic cream with and without abrasive particles was evaluated by using the difference in scores from the visual analogue scale (VAS) and Wong-Baker FACES Pain Rating Scales.

METHODS

The study was approved by the University of Pennsylvania institutional review board and was conducted as a single-site, double-blind, paired study. The objective of the study was to evaluate the efficacy of two types of BLT anesthetic creams which were composed of smooth and abrasive particles. All of the participants gave their written informed consent to the investigators before participating in the study. The result of the BLT cream was evaluated when applied for local anesthesia before injecting dermal fillers for augmentation of volume depletion/wrinkles.

Subject screening and enrollment. Thirty-one subjects were enrolled. Men and women over 18, but not more than 75 years of age, were included. Patients who have a regularly scheduled dermatology appointment for augmentation of their facial wrinkles were eligible for the study. The authors excluded any subject who had a previous history of allergy, sensitivity, and contraindication to benzocaine, lidocaine, and tetracaine. Patients with cardiac/respiratory disease, seizure disorder, and neuropathies, as well as patients who were under treatment for a dermatologic condition that may interfere with the evaluation of the study were also excluded. Pregnant women and women who were breastfeeding were excluded from the study. Women of childbearing potential were given a urine pregnancy test performed by members of the investigator team. Patients who reported concurrent use of anxiolytics and opiates, which may interfere with the interpretation of results, were excluded from the study. After agreeing to the consent form, these patients were enrolled in the study.

Procedure, questionnaire, and assessments. Participants were randomized to receive two types of BLT creams in a split-face fashion to two opposite anatomical face locations that require a similar amount of filler. Subjects were blinded to the type of BLT applied to each side of the face. One member of the team, the blind evaluator, was blinded to the site to which each type of BLT was applied. The study team applied BLT cream according to identification (ID) numbers chosen for each subject. Subjects with even numbered IDs had BLT with abrasives applied to the right of the face, and subjects with odd number study IDs had BLT with abrasive particles applied to the left side of the face. Both types of the cream were concurrently applied for 30 minutes to the designated treatment areas in a uniform thickness of approximately 1mm. After the face had been completely cleansed of BLT cream, the area was evaluated by the study team for signs of edema and erythema. A small 30-gauge needle point was used by the investigator to probe the level of the pain or discomfort. Subjects then received injections of HA by beginning with right nasolabial fold.

Upon first needle stick and upon completion of the injections at each site, subjects were asked to evaluate their pain and discomfort by using VAS and Wong-Baker Face Pain Rating Scale.

OUTCOME MEASUREMENTS

The subjects completed the VAS by drawing a single vertical line through a 10cm horizontal line. Following the completion of the study, the distance from the furthest left vertical axis (no pain) of the scale and the patient's VAS mark was measured in millimeters by using a ruler. Furthermore, patient's pain assessment was performed by using Wong-Baker Face Pain Rating Scale. This scale shows a series of faces ranging from a happy face at "no hurt" (0) to a crying face at "hurts worst" (10). At the same time, the VAS measurement was performed.

STATISTICAL EVALUATION

The authors evaluated the difference in the pain scale results between both types of BLT creams. All analyses were performed by SPSS version 13.0 (SPSS, Inc., Chicago, Illinois). Descriptive statistical analysis was used and differences among the mean pain levels as measured by the VAS and Wong-Baker Face Pain Rating Scale were analyzed by using the paired *t*-test.

RESULTS

Of the 31 subjects enrolled in the study, 28 (90%) were female. The mean age of the patients studied was 54 years old. More than half of subjects had a skin type of II or III (Table 1).

Table 2 shows a statistically significant difference ($P<0.05$) in the mean pain level as measured by the VAS and Wong-Baker Faces Pain Rating Scale when compared between baseline and the time when the procedure was started at the first needle stick. Subjects expressed significantly less pain with baseline and more pain when the procedure was done. However, the authors found that the mean pain level at first needle stick is lower with the abrasive type of BLT.

Table 3 shows the results when the authors compared the two groups of BLT—smooth versus abrasive creams. Although the application duration, area, and type of HA injection were identical in

both groups, they authors found no statistical difference in pain measurement between the two groups tested. They found that the mean VAS score was higher in the smooth base BLT cream. Likewise, the mean Wong-Baker Faces Pain Rating Scale is also higher in the smooth-based cream group. However, even though pain levels were higher at first needle stick injection in the smooth type cream on both VAS and the Wong-Baker Face Pain Rating Scale, the results were not statistically significant (P=0.786 and P= 0.231 respectively).

All adverse events (AEs) were recorded during the procedures. The investigators found that both types of BLT were well-tolerated and safe. Participants had no erythema, edema, or signs of allergic contact dermatitis. However, the authors reported erythema on the abrasive side in an Asian patient who had skin type III to IV (Figure 2).

Table 1. Patient demographics

	N=31	%
GENDER		
Female	28	90.32
Male	3	9.68
Race		
Caucasian	29	93.55
Native American	1	3.23
Asian	1	3.23
Ethnicity		
Hispanic	1	3.23
Mix	7	22.58
Other	23	74.19
Age, yrs.; Mean±SD (Min–Max) = 54.35±11.89 (34–78)		

DISCUSSION

Topical anesthetics were developed in the latter half of the 19th century and have taken nearly a century to readily develop.[8] Today, pain can be effectively alleviated in many dermatologic procedures by using topical anesthetics. Even in some procedures, such as laceration repair, which at one time requires the use of painful infiltrative anesthetics, can now be accomplished comfortably with the use of topical anesthetics.[9] However, concerns regarding pain potential in patients are still a main issue in such procedures as soft tissue augmentation with dermal fillers. Interestingly, more than half of subjects were concerned about associated pain with cosmetic procedures.[10] This result suggests that patient comfort is an important consideration during aesthetic procedures, especially in procedures requiring the use of needle-based injections, such as injectable HA dermal fillers.

Release of newer formulations of topical anesthetics with lidocaine may provide additional relief after the initial stick, but not the first needle-stick injection.[11] Several studies specifically have investigated mixing 2% lidocaine with HA prior to injection.[12] Recently, some research has been done about alternative methods of topical anesthesia when injecting dermal fillers, such as skin cooling through the use of cool air or ice. Ongoing research is devoted to developing effective topical anesthetics to minimize pain during injection of dermal fillers.[13]

The ideal topical anesthetics should safely increase patient comfort with minimal AEs. Choosing the proper topical anesthetic must be individualized

Table 2. Visual analog pain scale rated at baseline and at first needle-stick injection

	BASELINE	FIRST NEEDLE STICK	*p* VALUE
VISUAL ANALOGUE SCALE			
Smooth type			
Mean±SD	5.87±10.34	21.68±20.82	<0.001
Median (Min–Max)	2 (0–48)	14 (1–81)	<0.001
Abrasive type			
Mean±SD	5.65±10.29	20.52±23.29	<0.001
Median (Min–Max)	2 (0–51)	9 (0–79)	<0.001
WONG-BAKER FACES PAIN RATING SCALE			
Smooth type			
Mean±SD	0.55±0.68	1.74±0.89	<0.001
Median (Min–Max)	0 (0–3)	2 (0–4)	<0.001
Abrasive type			
Mean±SD	0.52±0.72	1.45±0.93	<0.001
Median (Min–Max)	0 (0–3)	1 (0–3)	<0.001

Table 3. Comparative result of mean pain scale between two groups of BLT by VAS and Wong-Baker Faces Pain Rating Scale

	SMOOTH MEAN±SD MEDIAN/(MIN–MAX)	ABRASIVE MEAN±SD MEDIAN/(MIN–MAX)	*p* VALUE
VISUAL ANALOGUE SCALE			
Baseline	5.87±10.34/2(0-48)	5.65±10.29/2(0-51)	0.499
First needle stick	21.68±20.82/14(1-81)	20.52±23.29/9(0-79)	0.786
End	9.48±18.77/2(0-92)	6.87±11.97/2(0-50)	0.400
WONG-BAKER FACES PAIN RATING SCALE			
Baseline	0.55±0.68/0(0-3)	0.52±0.72/0(0-3)	0.572
First needle stick	1.74±0.89/2(0-4)	1.45±0.93/1(0-3)	0.231
End	0.77±1.06/0(0-4)	0.61±0.88/0(0-3)	0.344
Paired *t*-test; significance ($p<0.05$)			

for different age groups, body locations, and dermatologic procedures. Many studies have evaluated topical anesthesia in various populations for various indications. It is commonly held that most topical anesthetics are safe, but compounded products should be prescribed specifically for individual patients and should not be mass produced. Compounded products may not be standardized and may contain concentrations of active ingredients that are higher than FDA-approved products. There have been numerous clinical trials evaluating FDA-approved product use for topical anesthesia in dermatologic procedures, such as the lidocaine/tetracaine cream (Pliaglis®, Galderma Laboratories, Fort Worth, Texas) and the lidocaine/prilocaine cream (EMLA® cream; lidocaine 2.5% and prilocaine 2.5%; AstraZeneca Pharmaceuticals, Westborough, Massachusetts).[5] To the authors' knowledge, there have been no head-to-head clinical studies of compounded products and these FDA-approved products. These compound medications typically contain higher concentrations of anesthetics than those found in FDA-approved products, and the result of the study may be inconsistent due to the variation of the mixtures prepared in independent compounding pharmaicies.[14]

Disruption of stratum corneum leads to enhancement of drug absorption and leads to faster onset of anesthesia.[15] Therefore, these patients can reach unpredictable high levels of anesthesia. Improper application of these compounded products, such as prolonged application or occlusion, use of inappropriately high concentrations, or use on an improper surface may cause serious complications, including

death. Difficulty may occur in dosing of these compounded products.[14] Kravitz reported that these compound products increased risk of AEs, such as overdose, because they have a low therapeutic index and may be improperly labeled. One of the most popular formulations of lidocaine-containing products used by cosmetic surgeons is BLT, which can cause serious AEs, including ocular injury. Because of their variation in texture, some dermatologists believe that the coarse texture with some abrasive particles would absorb better.[16] The authors' study does not prove that there is a statistically significant difference between the smooth and the abrasive type preparations.

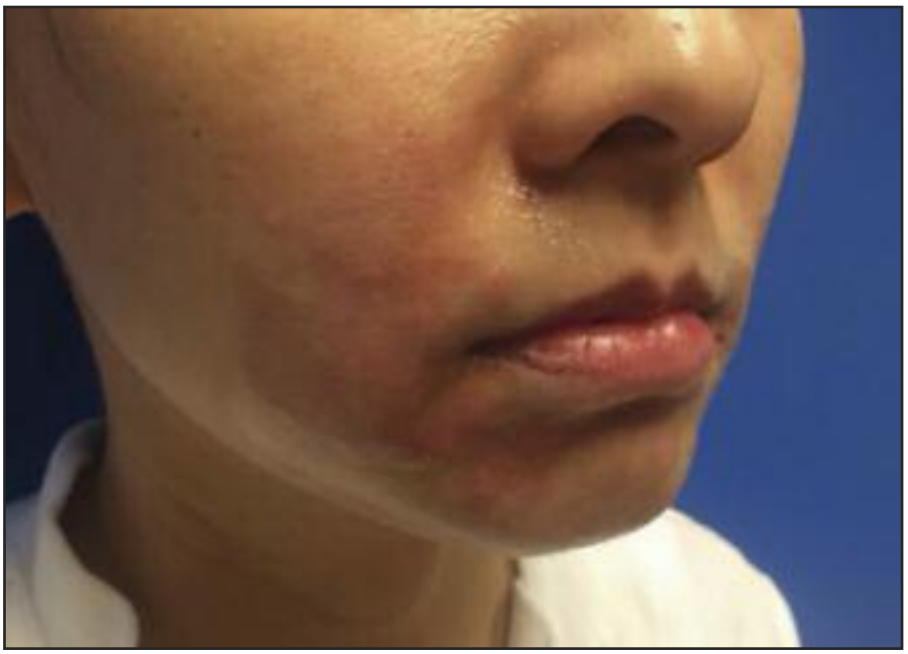

Figure 2. Erythema on the abrasive side of an Asian participant who had skin type III to IV

Allergic reactions are responsible for less than one percent of all adverse reactions to local anesthetics. Inciting allergens are composed of the anesthetic itself or their metabolic breakdown products or preservatives. Esters are more likely to cause allergic reactions due to the PABA metabolite.[17] Because the skin's keratinization acts as a major barrier to penetration of topical anesthetic, Berardesca et al proposed that ethnic differences in skin function may be responsible for skin reactivity in physiologic and pathologic conditions in terms of transcutaneous penetration and drug absorption.[18] As the authors found in their study, one participant who is Asian had a skin reaction to the abrasive type of BLT, which was not found in other participants who are Caucasian. However, localized edema, erythema, and blanching of the skin can be found in patients, which is considered to be due to pharmacological effects secondary to local vasodilatation.[19]

A limitation of this study is patient reporting. Fear and anxiety may bias pain reporting and interfere with attempts at measuring pain intensity via the VAS score and Wong-Baker Faces Pain Rating scale. Proper explanation and physical demonstration could reduce these emotional effects.[20]

In summary, the present study demonstrated that subjects experienced a higher mean pain level (but not statistically significant) when using the BLT with smooth texture compared to the BLT with abrasive particles when applied before HA dermal filler injection. These two types of anesthetic creams provided adequate pain management to patients. Allergic reaction was found in only one of 31 subjects (in an Asian patient), and it occurred on the side of the face where the abrasive BLT was used. Since application guidelines for using these types of compounded products are lacking, future studies are needed to develop compounded products as well as alternative methods to prevent patient discomfort during aesthetic injections.

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